

Notice of Allowability

Application No.

10/099,830

Examiner

Brandon J. Fetterolf, PhD

Applicant(s)

BURKE ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4/11/2006.
2. ☒ The allowed claim(s) is/are 34,41-44 and 48.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of the:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date <u>12/13/2004</u> | 7. <input type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

Information Disclosure Statement

The Information Disclosure Statement filed on 12/13/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

The rejection of claims 34, 41-44 and 48 under 35 U.S.C. 103(a) as being unpatentable over Friedlos et al. #1 (Biochem. Pharmacol. 1992; 44: 1739-1743, IDS) in combination with Norris et al. (Can. J. Chem. 1977; 55: 1687-1695) in view of Friedlos et al. #2 (Biochemical Pharmacology 1992; 44: 25-31, IDS) and Jaiswal (J. Biol. Chem. 1994; 269; 14502-14508, IDS) has been withdrawn in view of Applicants arguments and for the reasons set forth below.

As noted in the prior office action, Friedlos et al. #1 teach a method of treating a human target cell to be destroyed (MAWI-human colon carcinoma, see Materials & Methods, page 1739) comprising administering CB1954 and nicotinamide riboside (reduced) (NRH) or an analogue thereof (NADH) which is able to permeate the target cell membrane. Friedlos et al. further teach that CB1954 is an exceptionally potent anti-tumor agent in-vivo capable of curing the rat Walker 256 carcinoma (1st paragraph, line 1), but CB-1954 has not been successful for the treatment of human tumors because of the relative inactivity of human DT diaphorase (NQO1) towards CB1954 (page 1739, 2nd paragraph). Moreover, Friedlos et al. teach (page 1743, last paragraph) that such inactivity can be overcome by the addition of NADH resulting in enhanced cytotoxicity of CB1954 (see also abstract).

Friedlos et al. #1 do not explicitly teach or suggest a therapeutic system comprising a CB1954 and another reduced pyridinium derivative that are equivalents to the co-factors NRH or NADH in the reduction of CB1954 in a form for administration. Thus, while Norris et al. teach a dihydropyridine derivative, e.g., 1-carbamoylmethyl-3-carbamoyl-1,4,-dihydropyridine, which is encompassed by the instantly claimed compound of Formula I and Friedlos et al #2 teach that the simplest quaternary (and therefore reducible) derivative of nicotinamide, 1-methylnicotinaide, was as good of a co-factor as NAD(P)H, neither Norris et al. or Friedlos et al. #2 provides any motivation

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to combine CB1954 as taught by Friedlos et al. #1 with the dihydropyridine derivative taught by Norris et al. to arrive at the instantly claimed invention. As such, one of ordinary skill in the art would not have a reasonable expectation of success that the combination of CB 1954 and the dihydropyridinium derivative would function as claimed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
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BF
June 19, 2006


SUPERVISOR EXAMINER